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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,424	MIYAMOTO ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-8 and 12* is/are pending in the application.

4a) Of the above claim(s) *7,8 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/17/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the amendment, filed 3/17/2008, in which claims 4-5 and 9-11 were canceled, and claims 1, 2 and 6 were amended. Currently, claims 1, 2, 6-8 and 12 are pending.

Applicant's arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and objections not reiterated in this action have been withdrawn. **This action is FINAL.**

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 8/2/2007 is acknowledged.

Claims 7, 8 and 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/2/2007.

Claims 1, 2 and 6 are under consideration.

Information Disclosure Statement

Receipt of an information disclosure statement, filed on 3/17/2008, is acknowledged. The signed and initialed PTO 1449 has been mailed with this action.

Response to Arguments - Double Patenting (Warning)

The provisional objection of claim 10 is moot in view of Applicant's cancellation of the claim in the reply filed 3/17/2008.

Response to Arguments - Claim Objections

The objection of claims 1, 2, 4-6 and 9-11 has been withdrawn in view of Applicant's amendment to the claims in the reply filed 3/17/2008.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2 and 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection was made in the Office action mailed 10/18/2007 and has been rewritten to address the amendments to the claims in the reply filed 3/17/2008.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of

experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

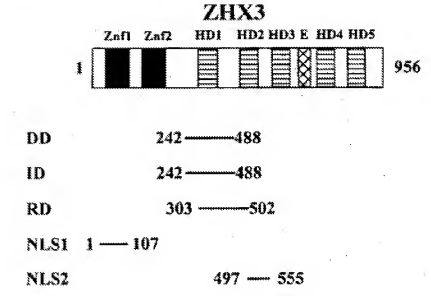
Nature of the invention: The claims are drawn to drugs to repress transcription of a gene expressed specifically in hepatoma cells. Thus, the nature of the invention is complex in that the claimed proteins must be capable of repressing genes specific to hepatoma, such as type II hexokinase and pyruvate kinase M, in a manner sufficient to have a therapeutic effect.

Breadth of the claims: Claims 1 and 6 are broadly drawn to drugs comprising a protein having "an amino acid sequence" of SEQ ID NO: 1. Thus, the protein is only required to have two contiguous amino acids in common with SEQ ID NO: 1. Further, claims 1 and 2 are broadly drawn to the repression of any hepatoma-specific gene. The complex nature of the subject matter of this invention is exacerbated by the breadth of the claims.

Guidance of the specification and existence of working examples: The specification asserts that it is known in the prior art that pyruvate kinase M gene and type II hexokinase gene are genes for the glycolytic pathway that are specifically induced in hepatoma (e.g., page 1). The specification states that NF-Y is a common transcription factor for both genes but is not differentially expressed between normal liver and hepatoma cells (e.g., page 1). Further, the specification teaches that ZHX1 interacts with NF-Y and is ubiquitously expressed (e.g., page 1).

The present specification teaches the identification of ZHX3 (SEQ ID NO: 1), which is a protein that interacts with ZHX1. The ZHX 3 protein contains the following domains:

Figure 14



ZHX3 contains two zinc fingers, five homeodomains, a glutamic acid-rich region (E), a dimerization domain for heterodimerization with ZHX1 and homodimerization, an interaction domain (ID) for interacting with NF-Y, a repression domain (RD), and nuclear localization sequences (NLS) (e.g., paragraph bridging pages 6-7; Figures 3, 6 and 14). The working examples of the specification demonstrate the ability of ZHX3 to interact with ZHX1 and NF-Y, the nuclear localization of ZHX3, and the ability of amino acids 303-502 to function as a transcriptional repression domain. As with ZHX1, ZHX3 is ubiquitously expressed (e.g., page 16, lines 17-22).

No working examples are provided that demonstrate the ability of any ZHX3 protein to treat hepatoma or to alter the expression of pyruvate kinase M gene or type II hexokinase gene in any model.

Predictability and state of the art: At the time the invention was made, it would have been an unpredictable venture to use a ZHX3 protein to treat hepatoma. There is no evidence on the record that ZHX3 expression is lost in hepatoma cell, nor is there evidence that provision of ZHX3 to hepatoma cells will result in any therapeutic effect, including the reduction of type II hexokinase and pyruvate kinase M. As disclosed in the present specification, the ZHX3 protein is a member of the ZHX family of proteins (e.g., page 2, lines 23-25). The post-filing art teaches that ZHX3 forms heterodimers with both ZHX1 and ZHX2 (Kawata et al. Gene, Vol. 323, pages 133-140, December 2003, cited in a prior action; e.g., Abstract; page 139, section 3.4). While the art is silent with regard to the expression and function of ZHX3 in hepatoma, the post-filing art teaches increased expression of ZHX2 in hepatoma (Zhang et al. Neoplasma, Vol. 54, No. 3, pages 207-211, 2007, cited in a prior action). Like ZHX1 and ZHX3, ZHX2 contains zinc fingers and homeoboxes and is a transcriptional repressor (Zhang et al, Abstract). Zhang et al studied the expression of ZHX2 protein in normal liver and 236 hepatocellular carcinoma (hepatoma, HCC) samples and found that ZHX2 protein is not expressed in normal liver but is expressed in HCC, with higher levels of expression in stage III-IV compared with stage I-II (e.g., paragraph bridging pages 207-208; page 210, Discussion; Table 1; Figure 1). ZHX2 protein expression was significantly higher in HCC cases with metastasis than without (e.g., page 210, right column, 2nd full paragraph). Thus, ZHX2 protein may take part in hepatocellular carcinogenesis and progression (e.g., paragraph bridging pages 210-211). Given the related structure and function and the heterodimerization of the ZHX family of proteins, it would be unpredictable to use any ZHX family member, including ZHX3, to treat hepatoma.

Amount of experimentation necessary: The quantity of experimentation required to determine how to use any claimed proteins to treat hepatoma is large, as the skilled artisan cannot rely upon the limited guidance provided by the present specification and prior art. One would be required to perform a large amount of trial and error experimentation to determine if SEQ ID NO: 1, and any of its fragments and variants, are capable of treating hepatoma or reducing the expression of hepatoma specific genes. Given the probable role of ZHX2 in hepatoma carcinogenesis and progression it would be unlikely for the related ZHX3 protein to function to reduce carcinogenesis and progression.

In view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the skilled artisan would have required an undue amount of experimentation to make and/or use the claimed invention. Therefore, claims 1, 2 and 6 are not considered to be enabled by the instant specification.

Claims 1, 2 and 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection was made in the Office action mailed 10/18/2007 and has been rewritten to address the amendments to the claims in the reply filed 3/17/2008.

Claim 1 is drawn to a protein comprising "an amino acid sequence" of SEQ ID NO: 1. Claim 1 is drawn to a genus of proteins that are only required to share two contiguous amino

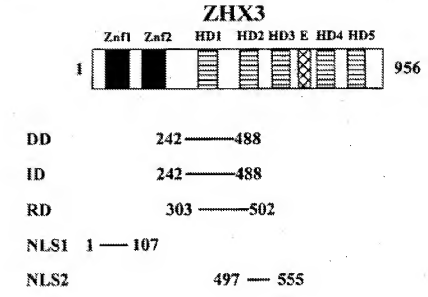
acids with the amino acid sequence of SEQ ID NO: 1. The genus of proteins must have the claimed function of repressing transcription of a gene expressed specifically in hepatoma cells.

Claim 2 is drawn to a protein comprising amino acids 303-502 of SEQ ID NO: 1. This portion of SEQ ID NO: 1 is the repression domain (Figure 14). The claimed protein is required to have the function of repressing transcription of a gene specifically expressed in hepatoma cells. This function requires localization of the protein to the gene (e.g., by a DNA binding domain or an interaction domain for a protein that specifically localizes to hepatoma-specific genes) and repression of transcription of the gene. However, the claim only specifies the structure for the repression function and does not specify the structure necessary to localize the repression domain to a gene expressed specifically in hepatoma cells.

Claim 6 is drawn to a protein of claim 1 or claim 2, where the gene is type II hexokinase or a pyruvate kinase M gene.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof. The specification describes the amino acid sequence of SEQ ID NO: 1, which is the human ZHX3 protein. The working examples of the specification define fragments 100% identical to portions of SEQ ID NO: 1 that function as a dimerization domain (DD), interaction domain (ID) for interacting with NF-Y, a transcriptional repression domain (RD) and two nuclear localization sequences (NLS).

Figure 14



It is noted that the interaction domain contains sequence outside the repression domain. Thus, the repression domain alone is not sufficient to target repression of a specific gene. The working examples of the specification demonstrate the ability of ZHX3 to interact with ZHX1 and NF-Y, the nuclear localization of ZHX3, and the ability of amino acids 303-502 to function as a transcriptional repression domain. The repression domain (305-502) was able to reduce the level of expression of a reporter gene when operably linked to a Gal4 DNA binding domain (e.g., pages 19-20, Example 5; Figure 12) The specification does not teach that the repression domain (305-502) is capable of repressing transcription without being operably linked to a DNA binding domain. No description is provided of structure necessary to reduce the expression of type II hexokinase and pyruvate kinase M. Further, there is no evidence of record that the ZHX3 protein is capable of treating hepatoma. There is no description of the specification of the structure necessary to treat hepatoma.

Even if one accepts that the examples described in the specification meet the claim limitations of the rejected claims with regard to structure and function, the examples are only representative of different domains of the protein of ZHX3. The specific structure of ZHX3 is not related to the function of reducing the expression of type II hexokinase and pyruvate kinase M and thus one would not know how to vary the structure of the protein of SEQ ID NO: 1 and provide the claimed activities.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of proteins, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18USPQ2d 1016.

"A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when … the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed." *In re Curtis*, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004). In the instant case, the

specification discloses the ZHX3 proteins of human (SEQ ID NO: 1) and rat (SEQ ID NO: 2) and teaches that they are 87.3% similar (e.g., 3, lines 4-10). However, it is unclear how the structure of ZHX3 in general relates to the function of modulating the expression of type II hexokinase and pyruvate kinase M and the treatment of hepatoma. Thus, if the full-length protein is capable of conferring these claimed properties, one cannot envision other structures that will have the same function.

Given the genus of proteins encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to structures necessary to regulate the expression of type II hexokinase and pyruvate kinase M to treat hepatoma, the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims. Thus, there is no structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision those proteins that satisfy the functional limitations of the claims. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the claimed invention for claims 1, 2 and 6.

Response to Arguments - 35 USC § 112

The rejection of claims 4-5 and 9-11 under 35 U.S.C. 112, second paragraph, is moot in view of Applicant's cancellation of the claims in the reply filed 3/17/2008.

The rejection of claims 1, 2 and 6 under 35 U.S.C. 112, second paragraph, has been withdrawn in view of Applicant's amendment to the claims in the reply filed 3/17/2008.

The rejection of claims 4-5 and 9-11 under 35 U.S.C. 112, first paragraph (enablement), is moot in view of Applicant's cancellation of the claims in the reply filed 3/17/2008.

With respect to the rejection of claims 1, 2 and 6 under 35 U.S.C. 112, first paragraph (enablement), Applicant's arguments filed 3/17/2008 have been fully considered but they are not persuasive.

At page 8, the response notes that the data provided in the declaration of Kazuya Yamada provides evidence that ZHX3 is capable of repressing the expression of pyruvate kinase M (PKM) and type II hexokinase (HKII) genes. The declaration provides evidence that the sequence of SEQ ID NO: 1 can repress transcription from the rat the rat PKM and HKII promoters in cells co-transfected with NF-Y protein. The declaration does not provide evidence that any other protein encompassed by claims 1 or 6 is capable of repressing transcription of PKM or HKII. The declaration does not provide evidence that amino acids 303-502 are sufficient for the repression of PKM or HKII expression. The declaration does not provide evidence that the claimed proteins can be used to treat hepatoma.

At page 9, the reply notes that ZHX3 transcriptional repressor activity of HKII and PKM genes is taught in the instant application at pages 1-3, Figures 9, 10, 11 and 12, Example 4, and the original claims. The Examiner is not questioning the ability of amino acids 303-502 of SEQ ID NO: 1 to functional as a transcriptional repression domain. Furthermore, the Examiner is not questioning the ability of the protein of SEQ ID NO: 1 to interact with NF-YA and regulate the expression of HKII and PKM. However, the claims are drawn to more than the use of amino acids 303-502 of SEQ ID NO: 1 as a generic repression domain. The claims require the domain to function to repress transcription of a gene expressed specifically in hepatoma cells. Amino

acids 303-502 of SEQ ID NO: 1 are not sufficient to carry out this function. For example, the specification teaches a GAL4 DNA-binding domain fusion protein comprising amino acids 303-502 of SEQ ID NO: 1; however, this protein binds to GAL4 binding sites and does not regulate the expression of a gene specifically expressed in hepatoma, as required by the claims. Furthermore, the claims encompass the use of proteins with only two contiguous amino acids in common with SEQ ID NO: 1 to regulate the expression of genes expressed specifically in hepatoma cells, including PKM and HKII. The evidence presented for the protein of SEQ ID NO: 1 cannot be predictably extrapolated to all of these sequence variants. Moreover, it would be unpredictable to use any of the claimed proteins for the treatment of hepatoma based on the observation of differential expression. As stated on pages 9-10 of the prior action, ZHX2 is not expressed in normal liver but is expressed in hepatoma, which higher levels of expression in stage III-IV compared with stage I-II, suggesting that ZHX2 may take part in hepatocellular carcinogenesis and progression. Given the related structure and function and the heterodimerization of the ZHX family of proteins, it would be unpredictable to use ZHX3 to treat hepatoma, when it may be contributing to the progression of the disease.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

With respect to the rejection of claims 1, 2 and 6 under 35 U.S.C. 112, first paragraph (written description), Applicant's arguments filed 3/17/2008 have been fully considered but they are not persuasive.

At page 8, the response asserts that Applicants describe a protein that is a transcriptional repressor as an effective component comprising an amino acid sequence of SEQ ID NO: 1 or comprising amino acids 303-502 of SEQ ID NO: 1. Thus, the response asserts that the instant specification allows a person of ordinary skill in the art to recognize the drug agents that are being claimed, and the recognition of what is being claimed suffices for compliance with the written description requirement. This is not found persuasive, because claims 1 and 6 encompass proteins with only two contiguous amino acids in common with SEQ ID NO: 1. The claimed structures are highly variable and are primarily defined by function, which is the ability to repress transcription of a gene expressed specifically in hepatoma cells. The description of the sequence of SEQ ID NO: 1 does not allow one to envision a representative number of species of this highly variable genus. While claim 2 requires all proteins to share amino acids 303-502 of SEQ ID NO: 1, and one skilled in the art would be capable of recognizing sequences containing amino acids 303-502 of SEQ ID NO: 1, this shared structural feature is not sufficient to confer the claimed function. For example, the specification teaches a GAL4 DNA-binding domain fusion protein comprising amino acids 303-502 of SEQ ID NO: 1; however, this protein binds to GAL4 binding sites and does not regulate the expression of a gene specifically expressed in hepatoma, as required by the claims. The claim does not specify the gene or sequences to which the claimed protein must bind, and thus one cannot envision a representative number of structures necessary to carry out the claimed function.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Response to Amendment – Declaration of Kazuya Yamada

The declaration under 37 CFR 1.132 filed 3/17/2008 is insufficient to overcome the rejection of claims 1, 2 and 6 based upon insufficiency of disclosure under 35 U.S.C. 112, first paragraph, as set forth in the last Office action because the evidence provided in the declaration is not commensurate in scope with the claims.

The declaration provides evidence that the sequence of SEQ ID NO: 1 can repress transcription from the rat the rat PKM and HKII promoters in cells co-transfected with NF-Y protein. The declaration does not provide evidence that any other protein encompassed by claims 1 or 6 is capable of repressing transcription of PKM or HKII. The declaration does not provide evidence that amino acids 303-502 are sufficient for the repression of PKM or HKII expression. The declaration does not provide evidence that the claimed proteins can be used to treat hepatoma.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (c) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Tang et al (WO 01/57190 A2, cited in a prior action; see the entire reference). This ground of rejection was rewritten to address the amendments to the claims in the reply filed 3/17/2008.

The claims are drawn to or encompass a protein having "an amino acid sequence" of SEQ ID NO: 1. The phrase "an amino acid sequence" is reasonably interpreted as encompassing any two or more contiguous amino acids of SEQ ID NO: 1.

Tang et al teach that isolated polypeptides are separated from their natural source and contain, if anything, only a solvent, buffer, ion, or other component present in a solution (e.g., page 11, lines 19-24). Tang et al teach an isolated polypeptide of SEQ ID NO: 3447 (e.g., page 28, lines 9-34; page 338). The amino acid sequence of SEQ ID NO: 3447 is 99% identical to instant SEQ ID NO: 1 (see the alignment in Exhibit I, mailed 10/18/2007). Because the amino acid sequence of SEQ ID NO: 3447 is 99% identical to the protein of SEQ ID NO: 1, it must contain a functional domain of the protein. Further, the high percent identity indicates that the protein of SEQ ID NO: 3447 would have the same function as instant SEQ ID NO: 1, such as the regulation of a type II hexokinase or pyruvate kinase M gene.

Claims 1 and 2 are rejected under 35 U.S.C. 102(e) as being anticipated by Isogai et al (US Patent No. 6,943,241 B2, cited in a prior action; see the entire reference). This ground of rejection was rewritten to address the amendments to the claims in the reply filed 3/17/2008.

The claims are drawn to or encompass a protein having "an amino acid sequence" of SEQ ID NO: 1. The phrase "an amino acid sequence" is reasonably interpreted as encompassing any two or more contiguous amino acids of SEQ ID NO: 1.

Isogai et al teach a purified polypeptide comprising the sequence of SEQ ID NO: 2005 (e.g., column 33, line 55 to column 34, line 53; Table 1 at column 6). The amino acid sequence of SEQ ID NO: 2005 is 100% identical to amino acids 300-956 of instant SEQ ID NO: 1 (see the alignment in Exhibit II, mailed 10/18/2007).

As disclosed in the instant specification, amino acids 303-502 of SEQ ID NO: 1 represent a transcriptional repression domain. Thus, Isogai et al teach a protein comprising amino acids 303-502 of SEQ ID NO: 1, which has transcriptional repression activity.

Response to Arguments

The rejection of claims 4 and 9-11 under 35 U.S.C. 102(b) as being anticipated by Tang et al is moot in view of Applicant's cancellation of the claims in the reply filed 3/17/2008.

With respect to the rejection of claims 1 and 6 under 35 U.S.C. 102(b) as being anticipated by Tang et al, Applicant's arguments filed 3/17/2008 have been fully considered but they are not persuasive.

The response essentially asserts that Tang et al do not disclose the functional properties of the protein encoded by SEQ ID NO: 1, such as the transcriptional repressor activity or usefulness for repressing PKM and HKII gene expression. This is not found persuasive, because something which is old does not become patentable upon the discovery of a new property. "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown

property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). In the instant case, the high percent identity between the protein of instant SEQ ID NO: 1 and the prior art protein of Tang et al indicates that the protein of Tang et al would have the same function as instant SEQ ID NO: 1, such as the regulation of a type II hexokinase or pyruvate kinase M gene, even if these properties were not recognized by Tang et al.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

The rejection of claims 4-5 and 9-11 under 35 U.S.C. 102(e) as being anticipated by Isogai et al is moot in view of Applicant's cancellation of the claims in the reply filed 3/17/2008.

With respect to the rejection of claims 1 and 2 under 35 U.S.C. 102(e) as being anticipated by Isogai et al, Applicant's arguments filed 3/17/2008 have been fully considered but they are not persuasive.

The response essentially asserts that Isogai et al do not disclose the functional properties of the protein encoded by SEQ ID NO: 1, such as the transcriptional repressor activity or usefulness for repressing PKM and HKII gene expression. This is not found persuasive, because something which is old does not become patentable upon the discovery of a new property. "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim

patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). In the instant case the instant specification teaches that amino acids 303-502 of SEQ ID NO: 1 represent a transcriptional repression domain. Isogai et al teach a protein comprising a sequence 100% identical to the claimed structure. Two identical structures necessarily have the same function.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached at 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

/JD/

/Celine X Qian Ph.D./
Primary Examiner, Art Unit 1636